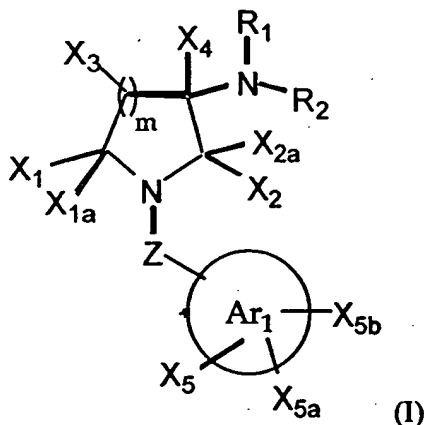
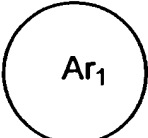


WHAT IS CLAIMED IS:

1. A compound of formula I



- 5 wherein  is a monocyclic heteroaryl group containing at least one nitrogen atom, or a bicyclic heteroaryl group which includes a first proximal ring that is attached to Z and a ring distal to said first ring, said distal ring including at least one nitrogen atom ;
- Z is alkylene, $-(CH_2)_rC(O)NR''(CH_2)_s-$, $-(CH_2)_sR''NC(O)(CH_2)_r-$, $-(CH_2)_rNR''(CH_2)_s-$ or $-(CH_2)_sNR''(CH_2)_r-$;
- 10 R_1 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R'O(CH_2)_x-$, $R'O_2C(CH_2)_x-$, $R'C(O)(CH_2)_x-$, $Y^1Y^2NC(O)(CH_2)_x-$, or $Y^1Y^2N(CH_2)_x-$;
- R' and R'' are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkenyl, optionally substituted heteroaralkenyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;
- 15 R_2 is hydrogen, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted aralkenyl, optionally substituted heteroaralkenyl, $R_3R_4NC(O)(CH_2)_x-$, $R_3S(O)_p-$ or $R_3R_4NS(O)_p-$;
- R_3 is hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl,

optionally substituted heteroaralkyl, optionally substituted aralkenyl or optionally substituted heteroaralkenyl, or R_1 and R_3 taken together with the $-N-S(O)_p-$ moiety or the $-N-S(O)_p-NR_4-$ moiety through which R_1 and R_3 are linked form a 5 to 7 membered optionally substituted heterocyclyl; and R_4 is hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl or optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form an optionally substituted 4 to 7 membered heterocyclyl;

X_1 and X_{1a} are independently selected from H, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, or X_1 and X_{1a} taken together form oxo;

X_2 and X_{2a} are H, or taken together form oxo;

X_3 is H, hydroxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or X_3 and one of X_1 and X_{1a} taken together form a 4 to 7 membered cycloalkyl;

X_4 is H, optionally substituted alkyl, optionally substituted aralkyl, or hydroxyalkyl;

X_5 , X_{5a} and X_{5b} are independently selected from H, R_3R_6N- , (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-,

R_7O- , R_5R_6NCO- , $R_5R_6NSO_2-$, R_7CO- , halo, cyano, nitro and $R_8(O)C(CH_2)_q-$, and when Ar_1 is a bicyclic heteroaryl group, one of X_5 , X_{5a} and X_{5b} is a substituent that is alpha to a nitrogen of said distal

ring of Ar_1 and is selected from the group consisting of H, hydroxy and H_2N- , (optionally substituted lower alkyl)HN (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-;

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Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl;

R_5 and R_6 are independently H or optionally substituted lower alkyl, or one of R_5 and R_6 is H and the other

5 of R_5 and R_6 is $R_8(O)CCH_2-$ or lower acyl;

R_7 is H, optionally substituted lower alkyl, lower acyl or $R_8(O)CCH_2-$;

R_8 is H, optionally substituted lower alkyl, alkoxy or hydroxy;

m is 0, 1, 2 or 3;

p and r are independently 1 or 2;

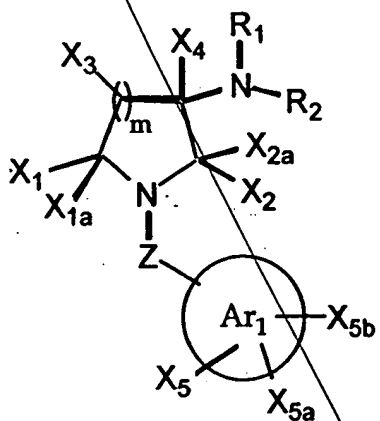
10 q is 0 or 1,

s is 0, 1 or 2; and

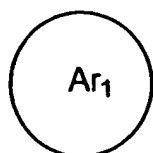
x is 1, 2, 3, 4, or 5, or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

15 2. A compound of formula I



(I), wherein



is a bicyclic heteroaryl which includes a first proximal ring that is attached to Z and a ring distal to said first ring, said distal ring including at least one nitrogen atom;

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Z is alkylene;

R₁ is hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, R'O(CH₂)_x-, R'O₂C(CH₂)_x-, Y¹Y²NC(O)(CH₂)_x-, or Y¹Y²N(CH₂)_x-;

R' is hydrogen, optionally substituted alkyl, optionally substituted aralkyl or optionally substituted heteroaralkyl;

R₂ is R₃S(O)_p- or R₃R₄NS(O)_p-;

R₃ is optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted heteroaralkyl, optionally substituted aralkenyl or optionally substituted heteroaralkenyl, or R₁ and R₃ taken together with the -N-S(O)_p- moiety or the -N-S(O)_p-NR₄- moiety through which R₁ and R₃ are linked form a 5 to 7 membered optionally substituted heterocyclyl; and

R₄ is optionally substituted alkyl, optionally substituted cycloalkyl or optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or R₃ and R₄ taken together with the nitrogen to which R₃ and R₄ are attached form an optionally substituted 4 to 7 membered heterocyclyl;

X₁ and X_{1a} are independently selected from H, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl or optionally substituted heteroaralkyl, or X₁ and X_{1a} taken together form oxo;

X₂ and X_{2a} are H, or taken together form oxo;

X₃ is H, hydroxy, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or X₃ and one of X₁ and X_{1a} taken together form a

4 to 7 membered cycloalkyl;

X_4 is H, optionally substituted alkyl, optionally substituted aralkyl, or hydroxyalkyl;

5 X_5 , X_{5a} and X_{5b} are independently selected from H, R_5R_6N -, (hydroxy, alkoxy or amino)HN-, R_7O -, R_5R_6NCO -, $R_5R_6NSO_2$ -, R_7CO -, halo, cyano, nitro or $R_8(O)C(CH_2)_q$ -, and one of X_5 , X_{5a} and X_{5b} is a

Ar_1

substituent that is alpha to a nitrogen of said distal ring of and is selected from the group consisting of H, hydroxy or H_2N -, (optionally substituted lower alkyl)HN (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-;

10 Y^1 and Y^2 are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heteroaralkyl, or Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl;

15 R_5 and R_6 are independently H or optionally substituted lower alkyl, or one of R_5 and R_6 is H and the other of R_5 and R_6 is $R_8(O)CCH_2$ - or lower acyl;

R_7 is H, optionally substituted lower alkyl, lower acyl or $R_8(O)CCH_2$ -;

20 R_8 is H, optionally substituted lower alkyl, alkoxy or hydroxy;

m is 0, 1, 2 or 3;

p is 1 or 2;

25

q is 0 or 1, and

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x is 1, 2, 3, 4, or 5, or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

Ar₁

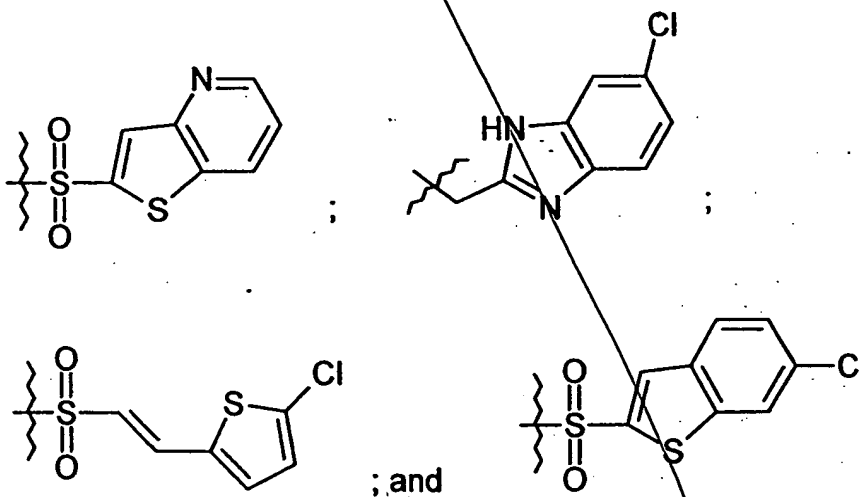
- 5 3. The compound of claim 1 wherein  is a monocyclic heteroaryl group containing at least one nitrogen atom.

4. The compound of claim 1 wherein Z is ~~alkylenyl~~, $-(CH_2)_rC(O)NR''(CH_2)_s-$, $-(CH_2)_sR''NC(O)(CH_2)_r-$, $-(CH_2)_rNR''(CH_2)_s-$ or $-(CH_2)_sNR''(CH_2)_r-$.

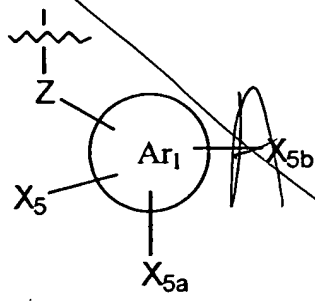
10

5. The compound of claim 1 wherein R₁ is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted aralkyl, optionally substituted heteroaralkyl, $R'O(CH_2)_x-$, $R'O_2C(CH_2)_x-$, $R'C(O)(CH_2)_x-$, $Y^1Y^2NC(O)(CH_2)_x-$, or $Y^1Y^2N(CH_2)_x-$.

- 15 6. The compound of claim 1 wherein R₂ is selected from the group consisting of

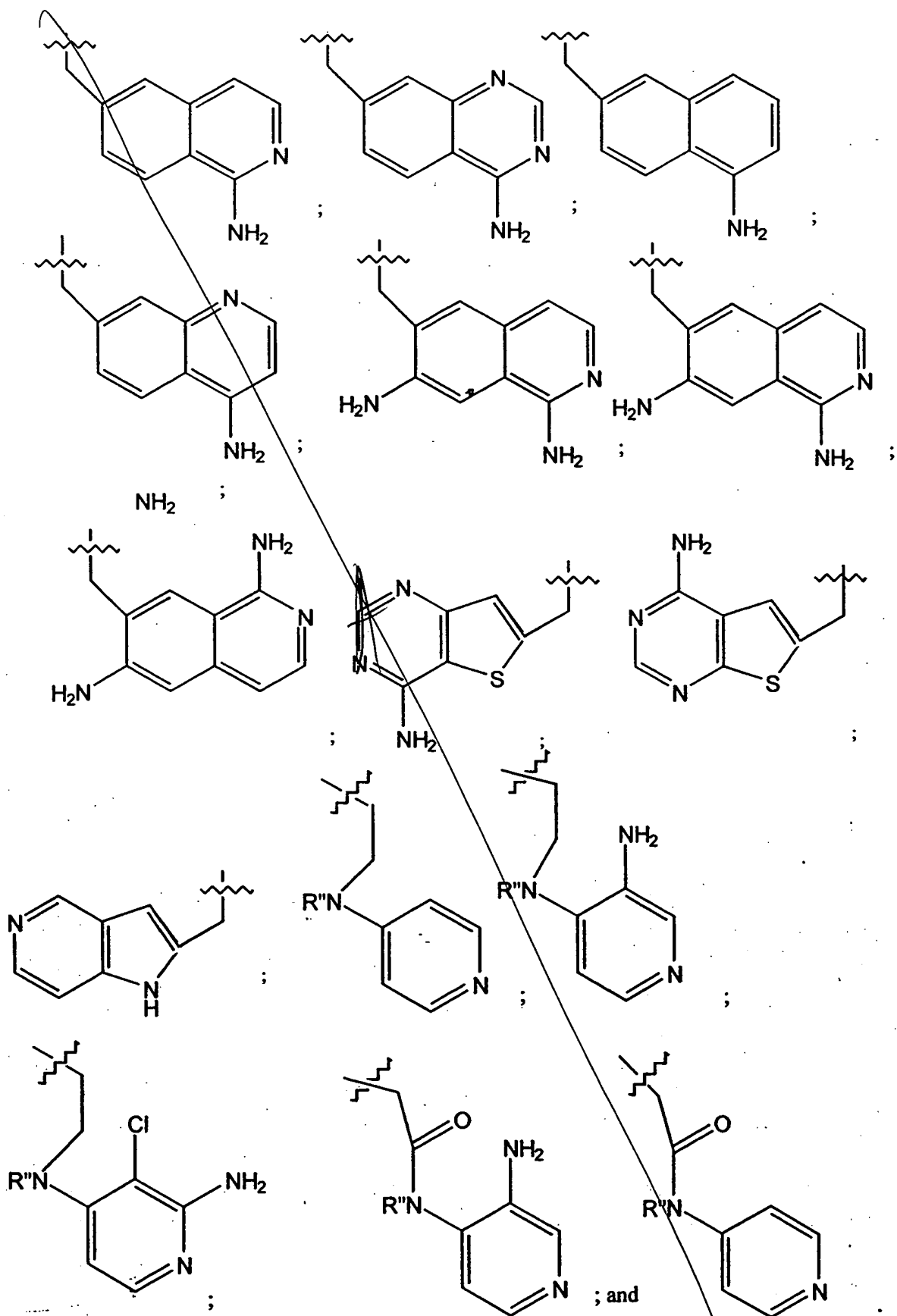


7. The compound of claim 1 wherein



is selected from the group consisting of

FIG. 4B



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8. The compound of claim 1 wherein R_1 is H, optionally substituted heteroaralkyl, optionally substituted aralkyl or optionally substituted alkyl.

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5 9. The compound of claim 1 wherein R_2 is $R_3S(O)_p$.

10. The compound of claim 9 wherein p is 2.

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10 11. The compound of claim 9 wherein R_3 is optionally substituted phenyl, optionally substituted naphthyl, optionally substituted thienyl, optionally substituted benzothienyl, optionally substituted thienopyridyl, optionally substituted quinolinyl, or optionally substituted isoquinolinyl.

12. The compound of claim 1 wherein Z is methylenyl and m is 1.

15 13. The compound of claim 1 wherein X_2 and X_{2a} taken together are oxo.

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14. The compound of claim 1 wherein each of X_1 , X_{1a} , X_3 and X_4 is H.

20

15. The compound of claim 1 wherein Ar^1 is optionally substituted isoquinolinyl.

16. The compound of claim 15 wherein Z is attached to isoquinolinyl at the 7-position thereof.

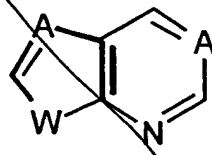
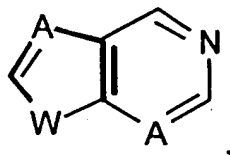
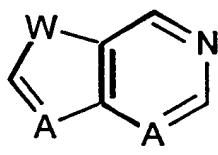
17. The compound of claim 1 wherein Ar^1 is optionally substituted quinolinyl.

25 18. The compound of claim 17 wherein Z is attached to quinolinyl at the 7-position thereof.

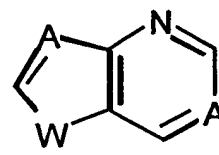
19. The compound of claim 1 wherein  is an optionally substituted quinazolinyl.

20. The compound of claim 19 wherein Z is attached to quinazolinyl at the 7-position thereof.

5 21. The compound of claim 1 wherein  is an optionally substituted moiety of formula



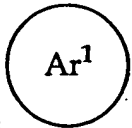
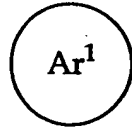
, or



and W is S, O or NR₁₁, wherein R₁₁ is H, alkyl, aralkyl, heteroaralkyl, R₈(O)C(CH₂)_q-, and A is CH or N.


10 22. The compound of claim 21 wherein Z is bonded to said moiety through the 5 membered ring.

23. The compound of claim 1 wherein one of X_s, X_{sa} and X_{sb} is a substituent that is on the proximal ring

15 of bicyclic , at a position that is alpha to where Z is attached to  and is selected from the group consisting of H, hydroxy and amino.

24. The compound of claim 23 wherein one of X_s, X_{sa} and X_{sb} is hydroxy or amino.

25. The compound of claim 1 wherein one of X_s, X_{sa} and X_{sb} that substitutes the distal ring of

20  at the position alpha to a nitrogen thereof is H or (H, optionally substituted loweralkyl, hydroxy or amino)HN⁺.

3-[[1-(4-Aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]-(5-chloro-1H-indol-2-ylmethyl)amino]propionic acid methyl ester;

1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[benzyl-(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;

1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)-(2H-pyrazol-3-ylmethyl)]amino]pyrrolidin-2-one;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(6-chlorobenzo[b]thiophen-2-ylmethyl)amino]pyrrolidin-2-one;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(6-chlorothieno[2,3-b]pyridin-2-ylmethyl)amino]pyrrolidin-2-one;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)amino]pyrrolidin-2-one;

3-~~{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-ylamino]methyl}~~-1H-quinolin-2-one;

1-(7-Aminothieno[3,2-b]pyridin-2-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;

~~2-(5-Chlorothiophen-2-yl)ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)pyrrolidin-3-(R)-yl]amide;~~

{[2-(5-Chlorothiophen-2-yl)ethenesulfonyl]-[2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)pyrrolidin-3-(R)-yl]amino}acetic acid isopropyl ester;

1-(4-Aminoquinolin-7-ylmethyl)-3-(R)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one;

5-Chloro-1H-benzoimidazole-2-sulfonic acid [1-(4-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-

yl]amide-7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;

**7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]
amide hydrochloride;**

7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]

amide trifluoroacetate:

7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(R)-yl]
amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(1-hydroxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R,S)-yl] amide;

7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R,S)-yl] methylamide trifluoroacetate;

5 7-Methoxynaphthalene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;

Benzo[b]thiophene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

10 6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(1-amino-6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide hydrochloride;

7-Methoxynaphthalene-2-sulfonic acid [1-(6-methoxyisoquinolin-7-ylmethyl)-2-oxo pyrrolidin-3-(S)-yl] amide trifluoroacetate;

15 4-(2-Chloro-6-nitophenoxy)benzene sulfonic acid [1-(1-amino-6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(1,6-diaminoisoquinolin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

20 6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1,6-diaminoisoquinolin-7-yl-methyl)-2-oxo pyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)yl] amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

25 Benzo[b]thiophene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;

30 7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide;

7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

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7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methyl amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methylamide;

5 7-Methoxynaphthalene-2-sulfonic acid [1-(2-aminoquinolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide;

7-Methoxynaphthalene-2-sulfonic acid [1-(2-hydroxyquinolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide;

7-Methoxynaphthalene-2-sulfonic acid [1-(1H-benzimidazol-5-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

10 7-Methoxynaphthalene-2-sulfonic acid [2-(1H-benzimidazol-5-ylethyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminoquinazolin-6-ylmethyl)-2-oxopyrrolidin-3-(S)-yl] methylamide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminothieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

15 7-Methoxynaphthalene-2-sulfonic acid [2-(6-aminothieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(7-aminothieno[2,3-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

20 7-Methoxynaphthalene-2-sulfonic acid [1-(7-hydroxythieno[2,3-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(4-aminothieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;

7-Methoxynaphthalene-2-sulfonic acid [1-(4-hydroxythieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;

25 Benzo[b]thiophene-2-sulfonic acid [1-(4-aminothieno[3,2-c]pyridin-3-yl-methyl)-2-oxopyrrolidin-3-(R,S)-yl] amide trifluoroacetate;

Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;

30 Thieno[2,3-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;

4-Pyridin-3-yl-thiophene-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S-yl)]-amide;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-thieno[2,3-d]pyrimidin-6-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;

15 5'-Chloro-[2,2']bithiophenyl-5-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-yl-methyl)-2-oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;

Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1,6-diamino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;

20 2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid N-((1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl)-amide;

5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S-yl)-amide;

25 3-(R)-5 Chlorothiophen-2-yl)-ethenesulphonic acid [1-(4-aminoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

2-(S)-[[1-(4-Amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-(6-chloro-benzo[b]thiophene-2-sulfonyl)-amino]-acetic acid methyl ester, trifluoroacetate;

2-(S)-6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(4-amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-
30 amide, trifluoroacetate;

2-(s)-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide, trifluoroacetate;

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Thieno[3,2-b]pyridine-2-sulfonic acid [1-(4-amino-quinolin-6-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide, ditrifluoroacetate;

N-(3-Amino-pyridin-4-yl)-2-[3-(7-methoxy-naphthalene-2-sulfonylamino)-2-oxo-pyrrolidin-1-yl]-acetamide;

5 2-[3-(7-Methoxy-naphthalene-2-sulfonylamino)-2-oxo-pyrrolidin-1-yl]-N-pyridin-4-yl-acetamide;

6-Chlorobenzo[b]thiophene-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-yl-amino)ethyl]-pyrrolidin-3-(S)-yl}-amide trifluoroacetate;

5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;

10 6-Chloro-thieno[2,3-b]pyridine-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide trifluoroacetate;

Thieno[3,2-b]pyridine-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide ditrifluoroacetate;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid {2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;

15 (S)-5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;

(S)-6-Chloro-benzo[b]thiophene-2-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;

20 ((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3(-yl)-amino)-acetic acid methyl ester;

((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid allyl-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;

25 6-Chloro-benzo[b]thiophene-2-sulfonic acid methyl-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide;

(S)-2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide trifluoroacetate;

30 (S)-Thieno[3,2-b]pyridine-2-sulfonic acid {1-[2-(2-amino-3-chloro-pyridin-4-ylamino)-ethyl]-2-oxo-pyrrolidin-3-yl}-amide ditrifluoroacetate;

[(2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid methyl ester;

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([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid isopropyl ester;

([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid trifluoroacetate;

5 2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (2-methoxy-ethyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amide trifluoroacetate;

([2-(5-Chloro-thiophen-2-yl)-ethenesulfonyl]-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-amino)-acetic acid ethyl ester trifluoroacetate;

3-(5-Chloro-thiophen-2-yl)-N-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3-yl}-acrylamide
10 trifluoroacetate;

1-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(4-chlorophenyl)urea trifluoroacetate;

N-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-2-(5-chlorothiophen-2-yloxy)acetamide
trifluoroacetate;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-indol-2-ylmethyl)amino] pyrrolidin-2-one
15 trifluoroacetate;

1-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(5-chlorothiophen-2-yl) urea
trifluoroacetate and 5-Chlorothiophene-2-carboxylic acid [1-(4-aminoquinazolin-7-ylmethyl)-2-
oxopyrrolidin-3-(S)-yl]amide trifluoroacetate;

{[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-[3-(5-chlorothiophen-2-
20 yl)acryloyl]amino}acetic acid methyl ester trifluoroacetate;

6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-
yl]amide trifluoroacetate;

Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide
trifluoroacetate;

25 1-(4-Aminoquinolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-indol-2-ylmethyl)amino]pyrrolidin-2-one
trifluoroacetate;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[3-(5-chlorothiophen-2-yl)allylamino]pyrrolidin-2-one
trifluoroacetate;

N-[1-(4-Aminoquinazolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-3-(5-chlorothiophen-2-yl)acrylamide
30 trifluoroacetate;

1-(4-Aminoquinazolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-benzimidazol-2-ylmethyl)amino]pyrrolidin-2-one
trifluoroacetate;

5-Chloro-benzo[b]thiophene-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

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Thieno[3,2-b]pyridine-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

5 5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

5-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

5-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

15 Thieno[3,2-b]pyridine-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[2,3-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

5'-Chloro-[2,2']bithiophenyl-5-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;

20 Thieno[3,2-b]pyridine-2-sulfonic acid [1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [(S)-1-(4-amino-thieno[3,2-d]pyrimidin-7-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide;

25 6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinolin-7-yl methyl)-2-oxo-3(R)-pyrrolidin-3-yl]amide trifluoroacetate; and

2-(5-Chlorothiophen-2-yl)-ethenesulfonic acid [1-(4-aminoquinazolin-7-yl methyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate.

30 27. A compound according to claim 1 which is selected from

7-Methoxynaphthalene-2-sulfonic acid[1-(6-methoxyisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(S)-yl]-amide trifluoroacetate;

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1-(4-Aminoquinolin-7-ylmethyl)-3-(S)-[(5-chloro-1H-benzimidazol-2-ylmethyl)amino]pyrrolidin-2-one trifluoroacetate;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [2-oxo-1-(1H-pyrrolo[3,2-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide;

5 2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid [1-(4-amino-quinazolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;

2-(5-Chloro-thiophen-2-yl)-ethenesulfonic acid (S)-[1-(4-amino-thieno[3,2-d]pyrimidin-6-ylmethyl)-2-oxo-pyrrolidin-3-yl]-amide trifluoroacetate;

10 Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-aminoisoquinolin-7-ylmethyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate;

6-Chlorobenzo[b]thiophene-2-sulfonic acid {2-oxo-1-[2-(pyridin-4-yl-amino)ethyl]-pyrrolidin-3-(S)-yl}-amide trifluoroacetate;

((6-Chloro-benzo[b]thiophene-2-sulfonyl)-{2-oxo-1-[2-(pyridin-4-ylamino)-ethyl]-pyrrolidin-3(-yl)-amino)-acetic acid methyl ester;

15 Thieno[3,2-b]pyridine-2-sulfonic acid [2-oxo-1-(1H-pyrrolo[2,3-c]pyridin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide ditrifluoroacetate;

Thieno[3,2-b]pyridine-2-sulfonic acid [1-(1-amino-isoquinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;

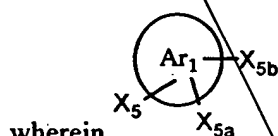
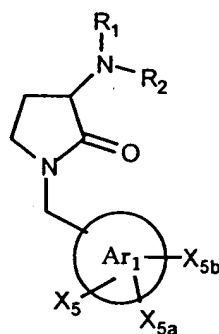
20 2(S)-(5Chloro-thiophen2-yl)-ethenesulfonic acid [1-(4amino-quinolin-7-ylmethyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide trifluoroacetate;

6-Chloro-benzo[b]thiophene-2-sulfonic acid [1-(1,6-diamino-isoquinolin-7yl methyl)-2-oxo-pyrrolidin-3-(S)-yl]-amide bistrifluoroacetate;

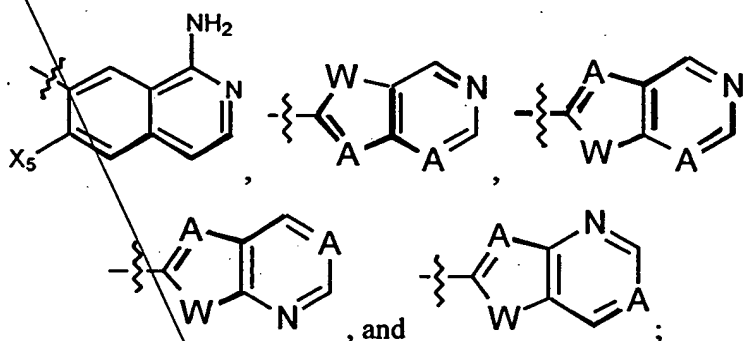
6-Chlorobenzo[b]thiophene-2-sulfonic acid [1-(4-aminoquinolin-7-yl methyl)-2-oxo-3(R)-pyrrolidin-3-yl]amide trifluoroacetate; and

25 2-(5-Chlorothiophen-2-yl)-ethenesulfonic acid [1-(4-aminoquinazolin-7-yl methyl)-2-oxopyrrolidin-3-(R)-yl]amide trifluoroacetate.

28. A compound according to claim 1 of the formula

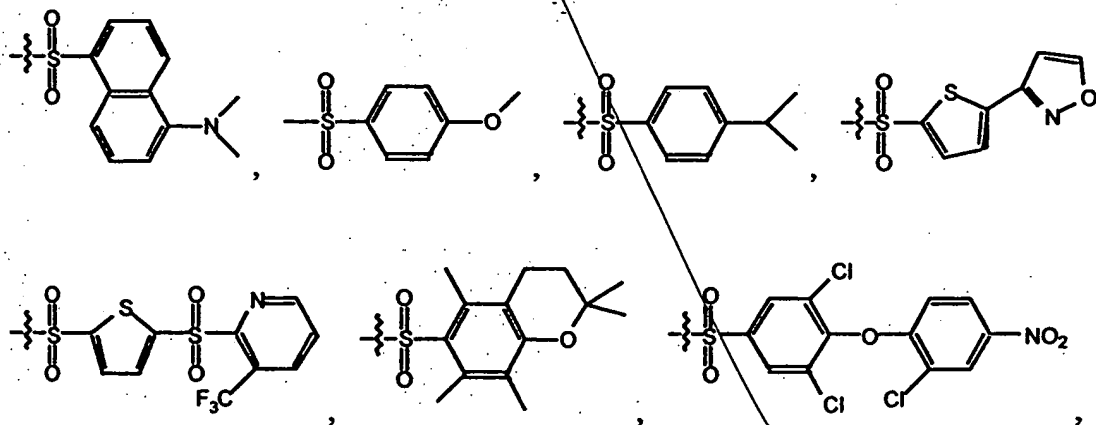
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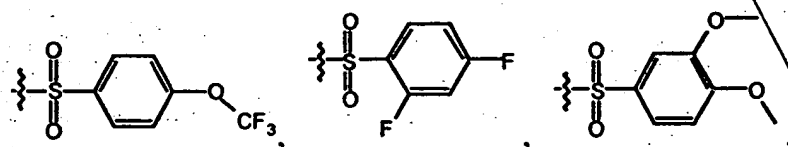
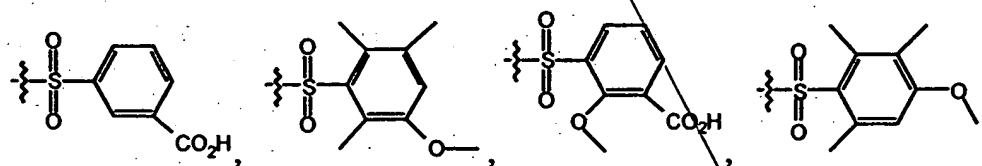
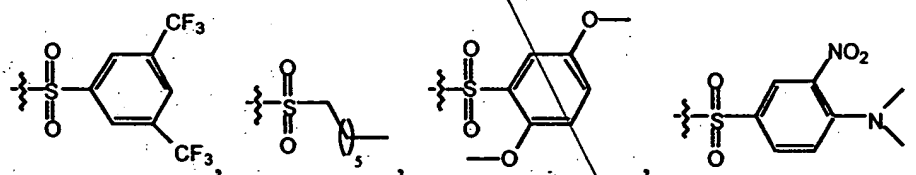
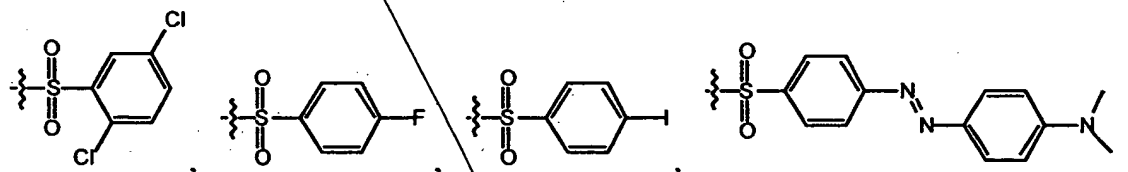
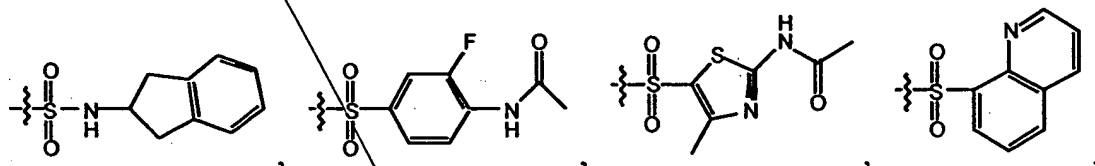
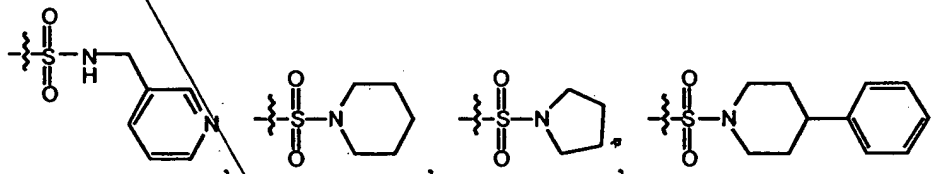
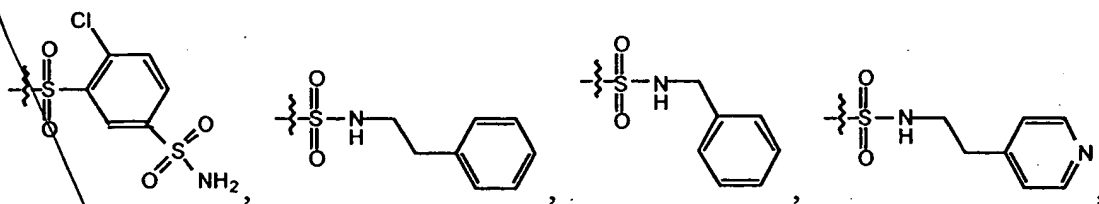
wherein Ar_1 is a radical selected from the group consisting of



W is S, O or NR_{11} , wherein R_{11} is H, alkyl, aralkyl, heteroaralkyl or

$\text{R}_8(\text{O})\text{C}(\text{CH}_2)_q$; A is CH or N; and R_2 is a radical selected from the group consisting of



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1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12. 13. 14. 15. 16. 17. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31. 32. 33. 34. 35. 36. 37. 38. 39. 40. 41. 42. 43. 44. 45. 46. 47. 48. 49. 50. 51. 52. 53. 54. 55. 56. 57. 58. 59. 60. 61. 62. 63. 64. 65. 66. 67. 68. 69. 70. 71. 72. 73. 74. 75. 76. 77. 78. 79. 80. 81. 82. 83. 84. 85. 86. 87. 88. 89. 90. 91. 92. 93. 94. 95. 96. 97. 98. 99. 100.

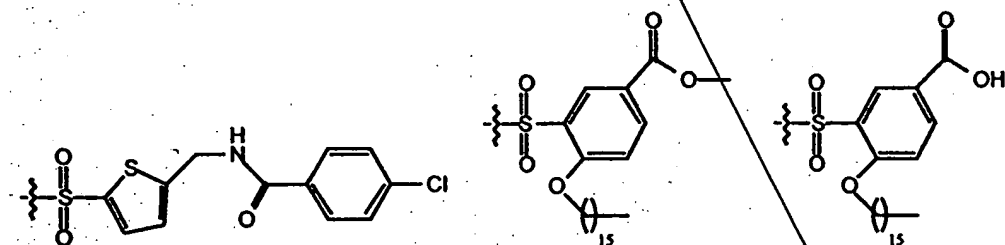
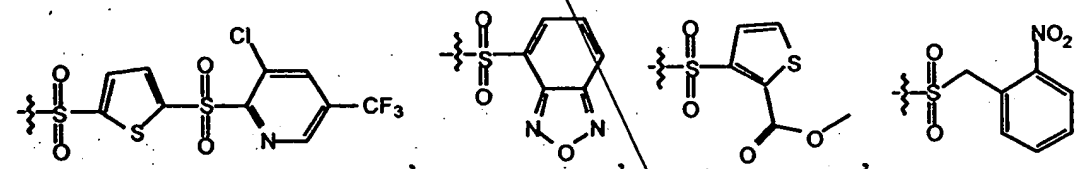
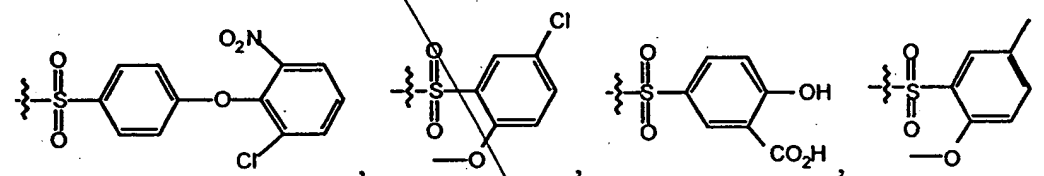
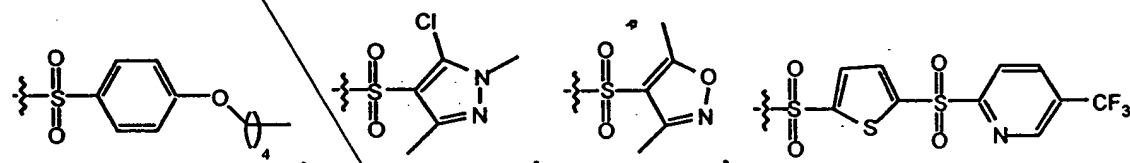
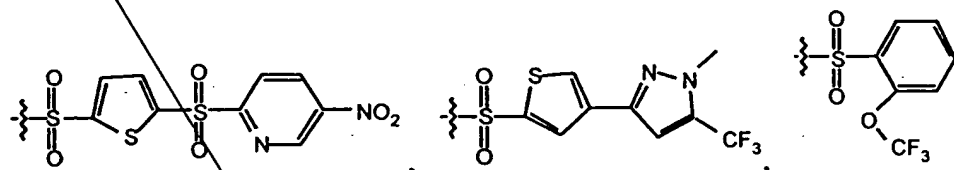
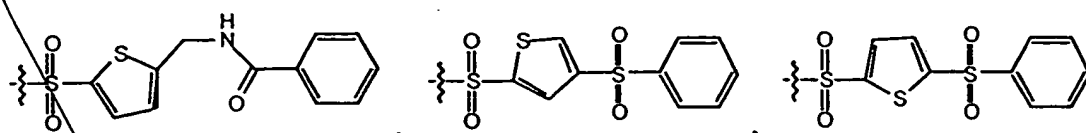
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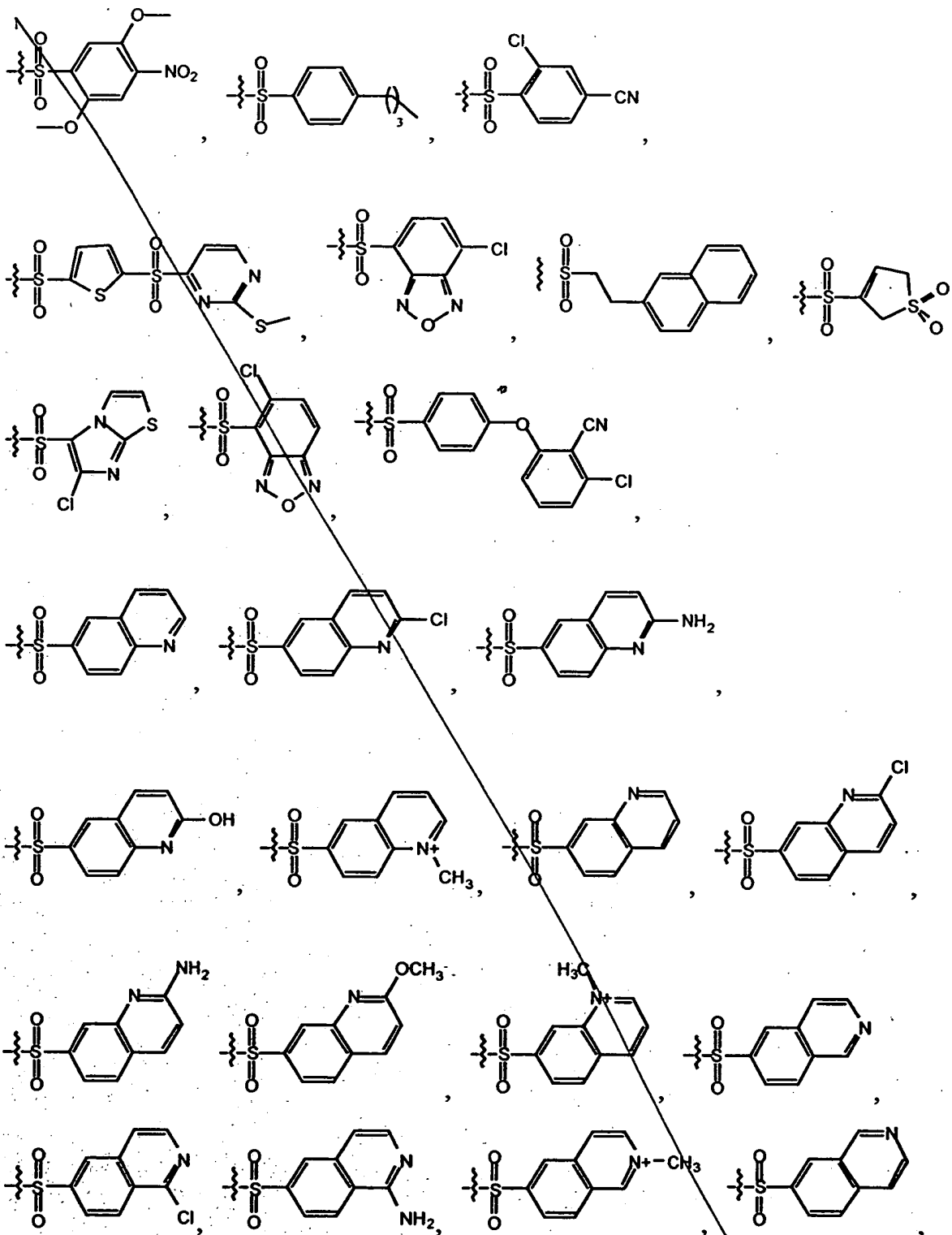


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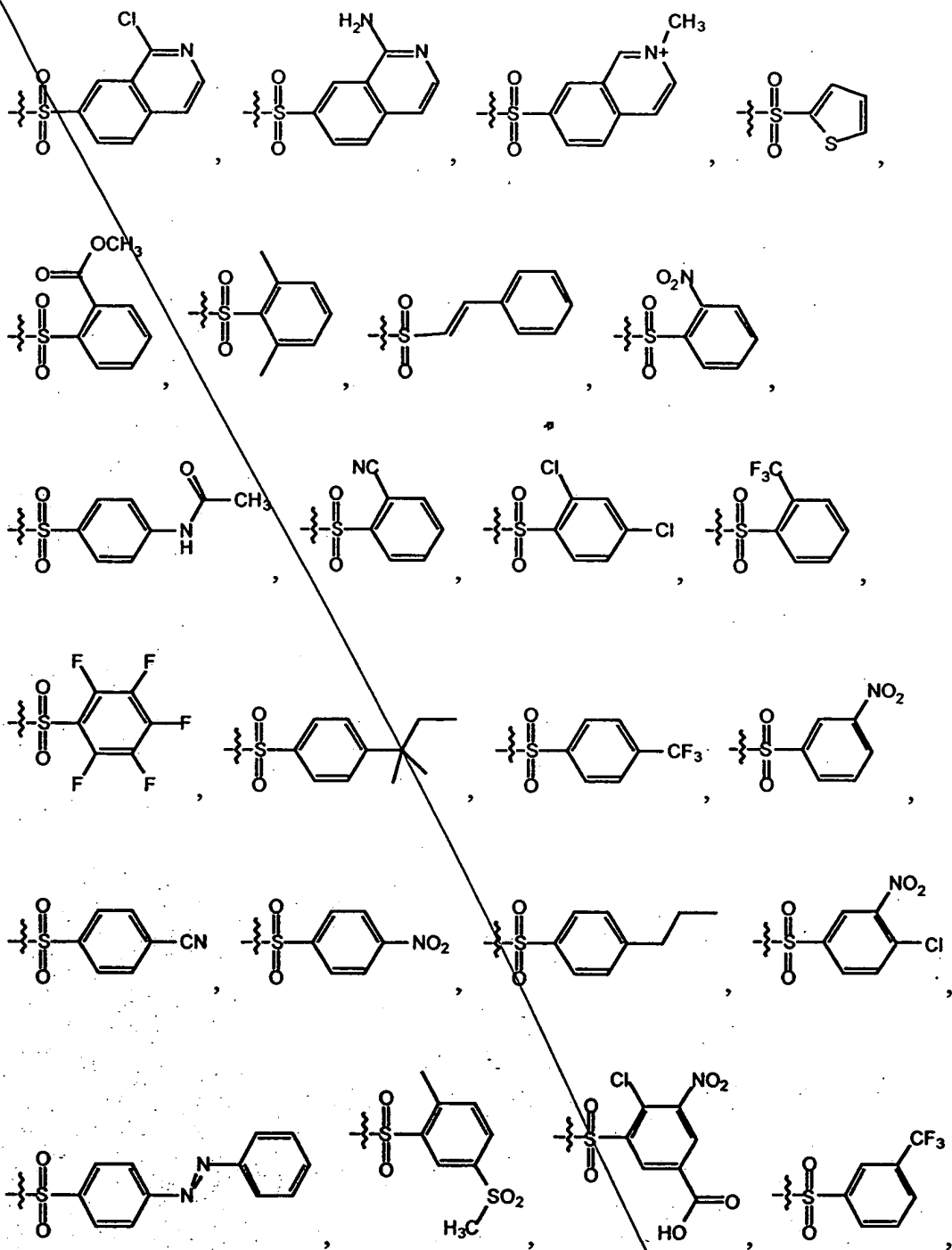


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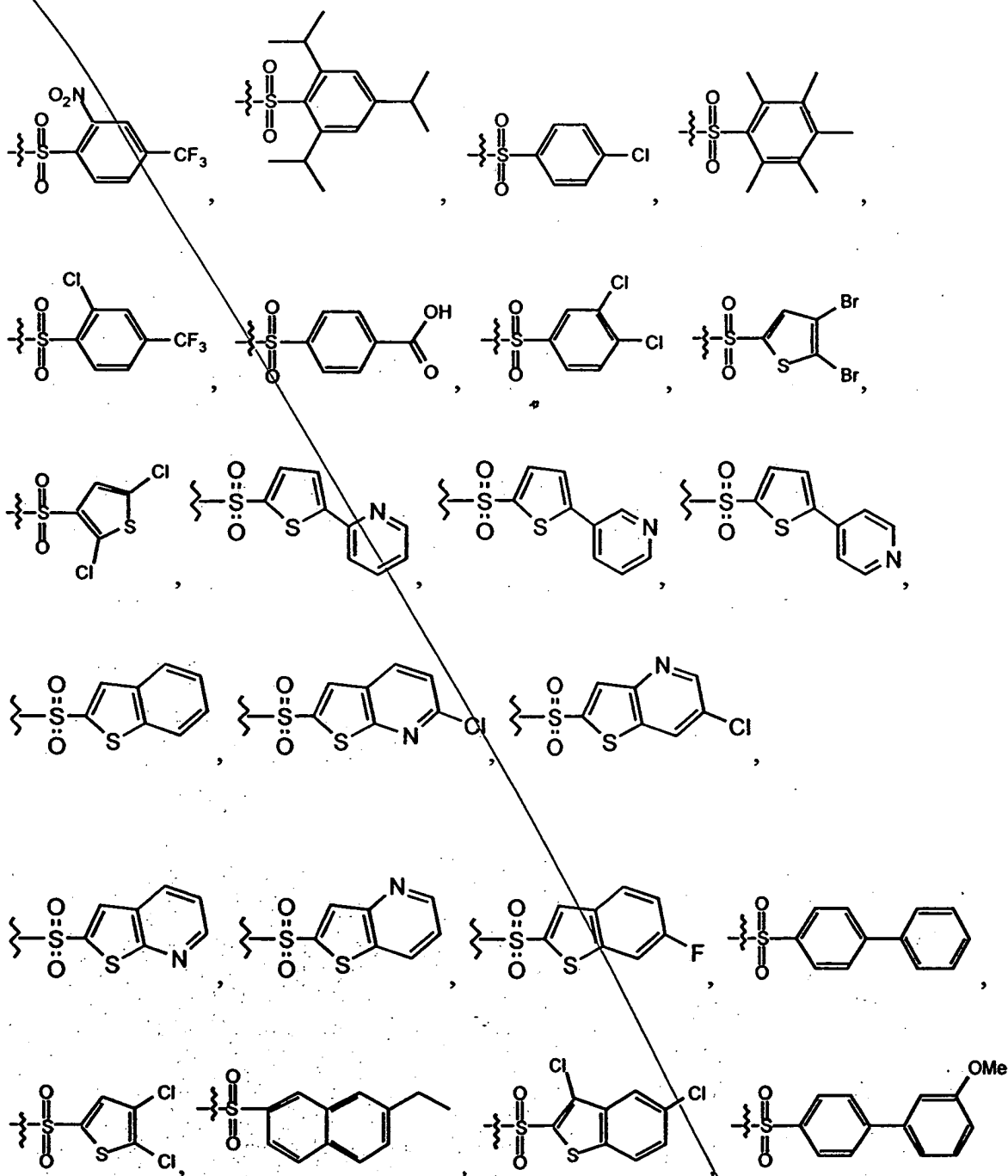


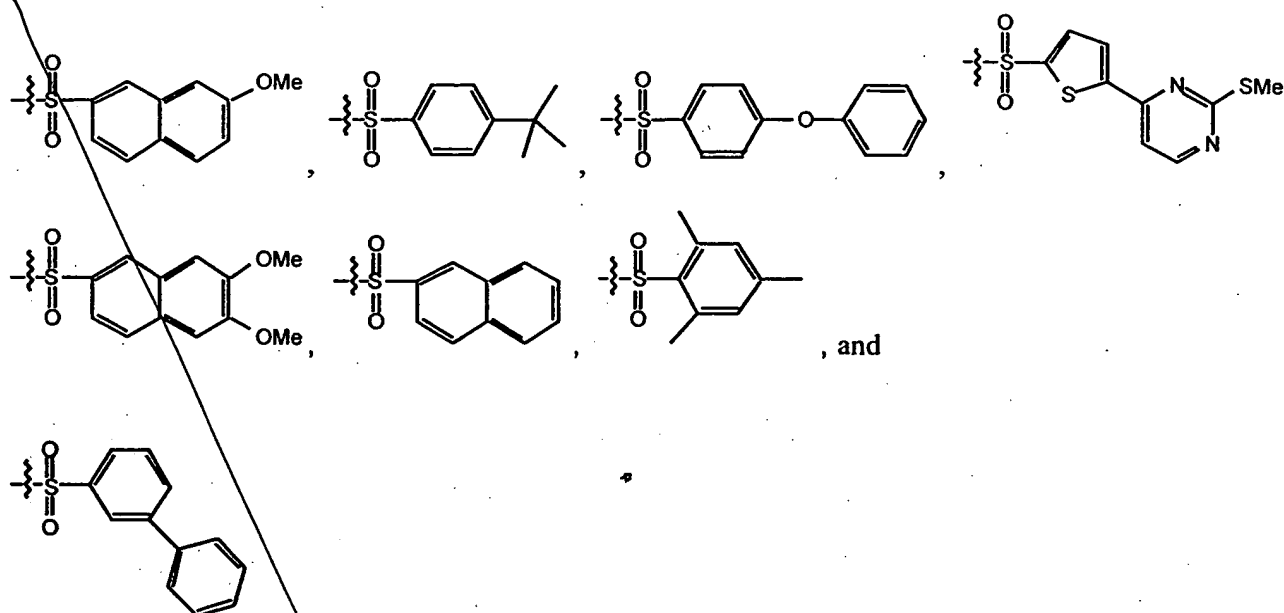
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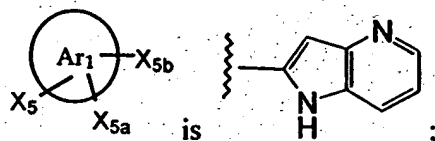
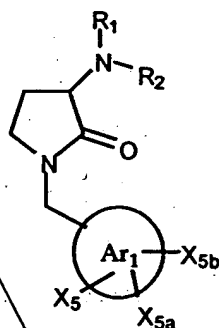
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29. A compound according to claim 1 of the formula

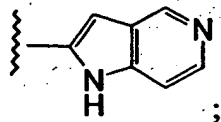
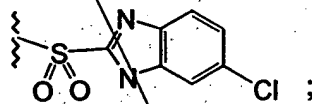
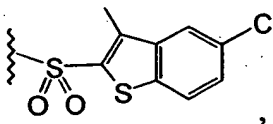
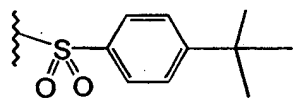
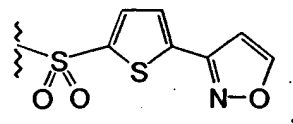
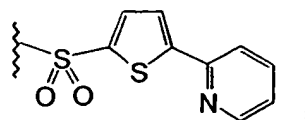


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wherein

R_1 is H; and R_2 is a radical selected from the group consisting of:

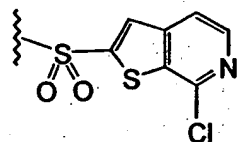
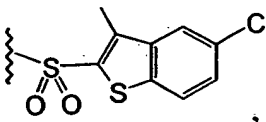
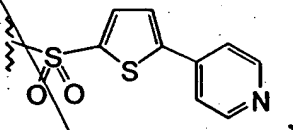
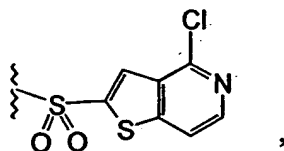
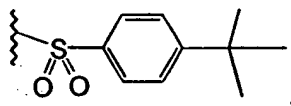
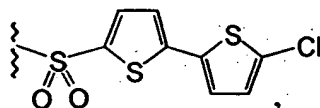
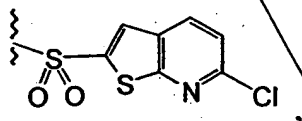
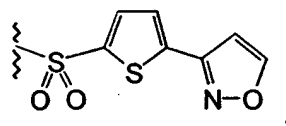
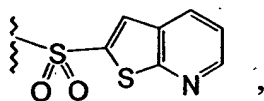
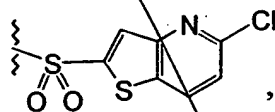
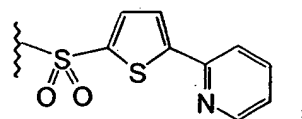
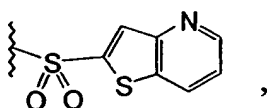
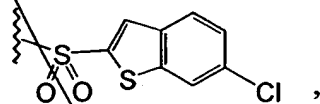
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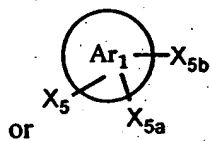
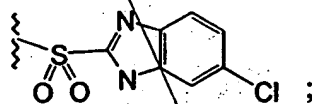
R₁ is H; and R₂ is a radical selected from the group consisting of:

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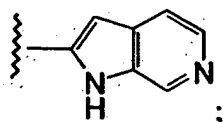
FIG. 6A



and

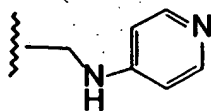
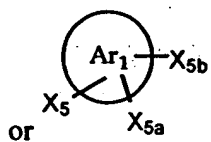
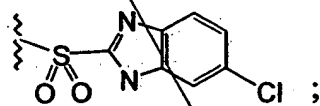
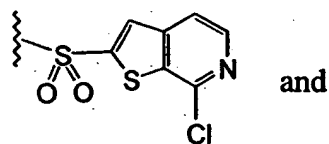
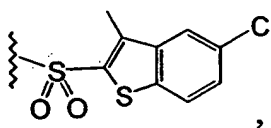
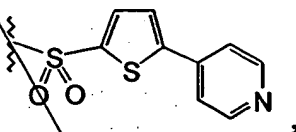
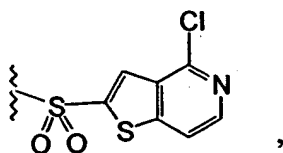
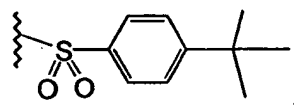
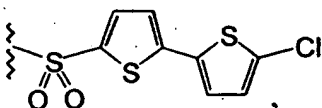
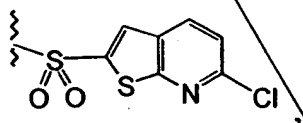
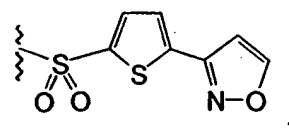
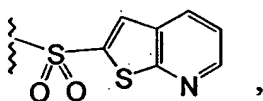
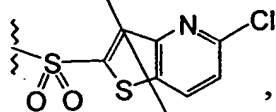
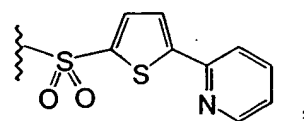
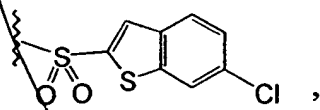


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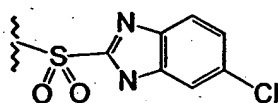


R_1 is H; and R_2 a radical selected from the group consisting of:

Sub
A6



R_1 is H; and R_2 is a radical selected from the group consisting of:



Sub
A6

[illegible]

31. A method for treating a patient suffering from a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa comprising administering to the patient a therapeutically effective amount of a compound according to claim 1.

Sub
B1

32. The method according to claim 31 wherein the physiological disorder is abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy or percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

Sub
Bl
33. The method according to claim 31 wherein the physiological disorder is abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, transient ischemic attacks, restenosis post coronary or venous angioplasty, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery or a risk of pulmonary thromboembolism.

34. The method according to claim 31 wherein the physiological disorder is stroke, vessel luminal narrowing, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

35. The method of claim 31 wherein said compound according to claim 1 is administered in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinolytic agents.

36. The method of claim 35 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

37. The method of claim 36 wherein said other agent is selected from direct thrombin inhibitors and fibrinogen receptor antagonists.

38. The method of claim 37 wherein said thrombin inhibitor is selected from boroarginine derivatives, boro peptides, hirudin, argatroban and the pharmaceutically acceptable salts, prodrugs, derivatives and analogs thereof.

39. The pharmaceutical composition of claim 30 further comprising at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinolytic agents.

5 40. The pharmaceutical composition of claim 39 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

41. The pharmaceutical composition of claim 40 wherein said other agent is selected from direct
10 thrombin inhibitors and fibrinogen receptor antagonists.

42. A kit for treating a patient suffering from a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa, said kit comprising a plurality of separate containers, wherein at least one of said containers contains a compound according to claim 1 and at least one other of said containers
15 contains at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinolytic agents, each of said containers optionally further containing a pharmaceutically acceptable carrier.